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Dated: October 21, 2003 Signature: _____ (Michael H. Teschner)

Docket No.: CIMA 3.0-035
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Patent Application of:
Holt, et al.

Application No.: 09/449,851 Group Art Unit: 1615

Filed: November 24, 1999 Examiner: Amy E Pulliam

For: TASTE MASKING RAPID RELEASE COATING SYSTEM

APPLICANTS' BRIEF ON APPEAL

MS Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Applicants hereby file this brief on Appeal in triplicate to appeal from the rejection of the primary examiner of claims 1, 4-18 and 21-25 mailed October 15, 2002, of the above-referenced application. The Notice of Appeal was filed on April 14, 2003. A petition for a five-month extension of the term for filing the brief to and including November 14, 2003, is transmitted herewith as is a proposed amendment pursuant to 37 C.F.R. § 1.116. The present brief is submitted with an authorization to charge the fee for filing the brief pursuant to 37 C.F.R. § 1.17(c) and any other necessary fees to a deposit account.

I. REAL PARTY IN INTEREST

The real party in interest for this appeal is the assignee CIMA LABS INC., a Delaware corporation with offices located in Eden Prairie, Minnesota.

II. RELATED APPEALS AND INTERFERENCES

No other appeals or interferences as specified in 37 C.F.R. § 1.192(c)(2) are known to appellant, to undersigned counsel, or to the assignee which will directly affect or be directly affected by or having a bearing on the Board's decision in the present appeal.

III. STATUS OF CLAIMS

By an official action mailed October 15, 2002 (paper number 26) the primary examiner indicated that claims 1, 4-18 and 21-25 are pending in the application and all have been rejected. This application contains claims that have been twice rejected.

IV. STATUS OF AMENDMENTS

All prior amendments have been entered and are reflected in the claims in Appendix A. An amendment is being filed concurrently with this Appeal Brief pursuant to 37 C.F.R. § 1.116 in order to place the claims in better form for appeal. Claims 1 and 14 are amended, and claims 4 and 21 are canceled. These amendments place the application in better condition for allowance and reduce the number of issues on appeal. The claims in Appendix A do not reflect the changes proposed in the amendment as same have not yet been entered. An updated Appendix will be filed if the Amendment is entered.

V. SUMMARY OF INVENTION

The invention of claim 1 relates to a taste masking formulation, which rapidly releases in the stomach of a patient. The formulation includes a drug containing core 11 (FIG. 1). The core can be a drug in powder, granule, matrix, absorbent or liquid form. (Specification at 6, lns. 5-6.) The core has a diameter of no larger than about 1500 microns. (Specification at 13, lns. 14-16.) A spacing layer 12 (FIG. 1) surrounds the drug containing core physically separating the core from a taste masking layer 13 (FIG. 1). (Specification at 6, lns. 8-11.) The taste masking layer and the spacing layer are selected to complement one another with respect to their drug release profile and taste masking ability. (Specification at 13, lns. 3-6.) The spacing layer that surrounds the core is made of a material that allows for rapid release of the drug once in the stomach of a patient. (Specification at 10, lns. 16-18.) Rapid release means that the spacing layer will pose little or no impediment to the otherwise normal dissolution and bioavailability of the drug if the drug were given in bulk form. The taste masking layer surrounds the spacing layer and core, and is composed of a material that is generally insoluble at a neutral to basic pH and completely soluble at a pH of less than about 6.5. (Specification at 11, lns. 24-26.) This allows the taste masking layer to be generally insoluble in normal saliva and completely and rapidly soluble in the stomach of a patient. The taste masking layer prevents or delays exposure of the spacing layer and the core for a period of time, *i.e.*, at least about 20 seconds. (Specification at 11, lns. 12-19.) The taste masking layer is

also capable of rapidly dissolving in the stomach, so that the spacing layer is exposed to the stomach quickly. (Specification at 11, lns. 7-9.) Once exposed, the spacing layer quickly dissolves and the drug containing core is exposed to the stomach.

In another aspect, the drug may be any pharmaceutically active material, vitamin, mineral, or nutritional supplement or mixture thereof. (Claim 5, Specification at 6, ln. 16 - p. 7, ln. 31.) Specific weights of the formulation, different thickness of the layers, and sizes of the core are also contemplated by the present invention. (Claims 6-13, and 22-23, Specification, *inter alia*, p. 9 ln. 22 - p. 10, ln. 2.)

Claim 14, an independent claim, encompasses an invention for a dosage form for direct oral administration. The dosage form includes an effective amount of at least one drug. The drug is in cores of coated particles. The coated drug containing cores generally have a diameter no larger than about 1500 microns. A spacing layer surrounds the cores, and a taste masking layer surrounds the spacing layer. The spacing layer and the taste masking layer are selected to complement one another in their drug release and taste masking abilities. The spacing layer completely sequesters the cores from the taste masking layer, and is capable of rapidly exposing the cores to the stomach when the spacing layer is exposed to the stomach. The taste masking layer also prevents the spacing layer from being exposed in the mouth of a patient for at least 20 seconds, but will disintegrate in the mouth in less than 90 seconds. The taste masking layer is composed of a material that is generally insoluble in a basic to neutral pH and completely soluble in a pH of less than about 6.5. The taste masking layer will rapidly expose the spacing layer when in the stomach of a patient, which in turn, will rapidly expose the core. The dosage form also includes at least one pharmaceutically acceptable excipient. (Specification at 12, ln. 30- p. 13, ln. 3.) This excipient may be, for example, binders, fillers, lubricants, bulking agents, colorants, flavor absorbates, anti-tack agents, fillers, plasticizers, pore forming agents, or glossing agents. (Specification at 9, lns. 13-16.)

Some further aspects of present invention include the coated particles weighing between greater than zero and 95% of the finished dosage form's weight, and more preferably, weighing between greater than zero and 75%. (Claims 15-16, Specification, at 14, lns. 14-17.) The dosage form may additionally include a disintegrant. (Claims 17-18, Specification at 9, lns. 13-16.) Because applicants have offered to cancel claims 4 and 21, they are not discussed.

VI. ISSUES

Was the Examiner's rejection of claims 1, 4-18 and 21-25 under 35 U.S.C § 103(a) over Kais *et al.*, U.S. Patent 5,516,514 ("*Kais*") correct?

VII. GROUPING OF CLAIMS

With respect to the rejection on *Kais*, separate arguments are presented with respect to each of the following groups of claims:

Group I: Claims 1, 5 and 14

Group II: Claims 6, 7, 10 and 11

Group III: Claims 8, 9, 12 and 13

Group IV: Claims 15 and 16

Group V: Claims 17 and 18

Group VI: Claims 22-25

The claims of these individual groups are believed to be separately patentable, and do not stand or fall with the claims of other groups. However, if the claims of Group I are found patentable, all of the claims in all of the groups should be patentable as well.

VIII. ARGUMENT

A. Group I: Claims 1, 5 and 14

The examiner rejected claims 1, 5 and 14 under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent 5,516,524 to Kais. Applicants respectfully maintain that the examiner did not carry the Patent Office's burden of establishing a *prima facie* case of obviousness.

Kais is directed to a composition and process for an ingestible, neutral tasting laxative containing bulk fiber. The laxative includes dioctyl sulfosuccinate, which has a particularly bitter taste. The coating of the *Kais* invention allegedly prevents a bad taste in the mouth, and can be specifically selected so that it "remains largely intact through the stomach, thereby avoiding gastric disturbances which are commonly associated with the use of dioctyl sulfosuccinate as a medicinal drug." (*See Kais*, col. 5, lns. 20-25.) In one embodiment, this is achieved through a double coating that can be selected from C_{14-18} fats, C_{16-20} fatty acids, sucrose polyesters, C_{14-18} fats and waxes, pH sensitive polymers, food gums, and combinations thereof. (*See Kais*, col. 5, lns. 57-61.) The two

coatings can be selected from among the same materials, but it is preferred that the two coatings are different such that one coating does not have any appreciable amount of material in common with the other coating. (*See Kais*, col. 5, lns. 61-65.) In particular, the pH sensitive coating can be selected so that it does not dissolve until it is in a specific pH environment, preferably the basic environment of the small intestine. (*See Kais*, col. 5, lns. 45-47.) *Kais* contains one example, Example VII, where a pH sensitive coating is used as part of a two coating system, and the pH sensitive coating is the inner, or "barrier" coating only, and not the outer, or "protective" coating. (*See Kais*, col. 12, lns. 35-67.)

In rejecting the claims on appeal, the examiner has stated:

> Specifically, Kais is relied upon for the teaching that double coatings are used for taste masking... Further, Kais teaches that the second coating can be chosen from pH sensitive polymers.

Official Action, Paper No. 26, at p. 2. The examiner states that *Kais* uses Eudragit E as an example of a pH sensitive polymer, further noting that the application on appeal uses Eudragit E as an example for the taste masking layer. *Id.* at 2-3. The examiner notes that the specific weights and thicknesses of the coatings are not disclosed in *Kais*. However, the examiner argues that these limitations would be routinely determined by one of ordinary skill in the art. *Id.* at 3. Also, the examiner states that while *Kais* does not specify any drug core diameter, this limitation is a manipulatable limitation determined as part of the process of normal optimization, and that *Kais*' core size may be the same. *Id.* The examiner concludes:

> One of ordinary skill in the art would have been motivated to make a dual coated particle with Applicants' limitations, based on the teachings of *Kais*.

Id. at p. 4.

Applicants respectfully disagree. It is applicants' position that the examiner has failed to carry the Patent Office's burden of establishing a *prima facie* case of obviousness based on *Kais*. Indeed, applicants will show such a case cannot be established on the present record.

1. The Examiner Has Not Met Her Burden Of Establishing A *Prima Facie* Case Of Obviousness Using *Kais*.

The examiner has failed to establish a *prima facie* case of obviousness. Three criteria must be met to establish a *prima facie* case of obviousness: first, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of

ordinary skill in the art, to modify the reference or to combine reference teachings; second, there must be a reasonable expectation of success; and third, the prior art reference must teach or suggest all the claim limitations. *See* M.P.E.P. § 2142. The examiner has failed to show the first and third requirements for a *prima facie* case of obviousness.

Kais does disclose that two coatings may be used. One of many types of coatings that may be used according to *Kais* is a pH sensitive coating. However, the similarity between *Kais* and the claimed invention ends there. *Kais* says nothing about the order of coatings, the amount of coating, the size of the drug core(s), or the need for rapid exposure of the core(s) in the stomach. Clearly, no *prima facie* case of obviousness has been established.

a. Kais does not teach or suggest all of the claim limitations of the claims of Group I

"To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art." *See* M.P.E.P. § 2143.03 (*citing In re Royka*, 490 F.2d 981 (CCPA 1974)). *Kais* does not teach all the limitations of the claims of Group I. The claims of Group I require an outer taste masking layer which is generally insoluble in saliva at a neutral to basic pH and completely soluble at a pH of less than about 6.5, which is capable of rapidly exposing the spacing layer once in the stomach of a patient. The claims of Group I also require a spacing layer surrounding a drug containing core that is capable of rapidly exposing the core when exposed to the stomach of a patient. *Kais* does not teach the need or desirability of using <u>two</u> coatings that will meet these criteria and rapidly release in the stomach of a patient.

Kais teaches or suggests double coating formulations to mask the taste of dioctyl sulfosuccinate. *Kais* teaches or suggests six broad categories of materials to use for one or in some cases two coatings without directing one to any particular coating or group of coatings. While one of the broad categories identified in *Kais* is a pH sensitive coating, *Kais* does not teach using two pH sensitive coatings together, two coatings that are acid sensitive or two coatings, the outermost of which must be resistant at neutral to basic pH for the amount of time described and claimed. Indeed, *Kais* does not teach or suggest how to select the two coatings other than to state that the two coatings should preferably not be of the same material. The claims in Group I of applicants' invention have limitations that there be two coatings, one on the outside that will dissolve at a pH less than about 6.5 and, the other on the inside that will rapidly release once in the stomach. These limitations of the claims of Group I are not taught or suggested in *Kais*. Thus, the examiner has failed to establish a *prima facie* case of obviousness.

b. *Kais* fails to teach, suggest or motivate a taste masking formulation having two coatings that are selected such that they will dissolve in specific pH environments and release the drug containing core in the stomach of a patient

A *prima facie* case of obviousness requires teaching, suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art to modify the reference. *See* M.P.E.P. § 2142. In a recent case, the Court of Appeals for the Federal Circuit has stated:

> Thus, every element of a claimed invention may often be found in the prior art. However, identification in the prior art of each individual part claimed is insufficient to defeat patentability of the whole claimed invention. Rather, to establish obviousness based on a combination of the elements disclosed in the prior art, there must be some motivation, suggestion or teaching of the desirability of making the specific combination that was made by the applicant. Even when obviousness is based on a single prior art reference, there must be a showing of a suggestion or motivation to modify the teachings of that reference.

In re Kotzab, 217 F.3d 1365, 1369-70; 55 U.S.P.Q.2d (BNA) 1313, 1316-17 (Fed. Cir. 2000) (citations omitted).

Kais does not motivate, suggest, or teach a taste masking formulation having two coatings each selected such that they will dissolve in specific pH environments and release the drug containing core in the stomach of a patient. *Kais* suggests double coating formulations with a large selection of materials for potential coatings, many of which are not pH sensitive. Among this large selection of materials for potential coatings, there are six broad classes of materials that are listed, with pH sensitive coatings being only one of the six broad categories. And *Kais* does not place any emphasis on which coatings should be selected or which order they should be used. Even within the category of pH sensitive coatings, there is nothing in *Kais* to suggest that only coatings that perform a certain way in specified pH ranges should be used. According to *Kais*, a coating which was insoluble at acidic pH and one was insoluble at basic pH are equally useful. Such is not the case for the claimed invention.

In fact, if anything, *Kais* teaches away from Applicants' invention by concerning itself only with delivering dioctyl sulfosuccinate to the large intestine achieved by keeping at least one coating intact through the stomach. *Kais* also only has one example using a pH sensitive coating, Example VII, which uses a pH sensitive coating on the inside and protective cellulosics as the outside coating. Therefore, the only suggestion from the examples as to pH sensitive coatings is to

use a single pH sensitive coating on the inside and not the outside. Moreover, that coating should not dissolve in the stomach rapidly exposing the core(s) as claimed. Certainly, the examples of *Kais* do not teach, suggest, or motivate the Applicants' invention.

There is no teaching, suggestion or motivation in *Kais* that the pH sensitive coating should be used on the outside and, further still, in combination with another pH sensitive coating on the inside which will rapidly expose the core in the stomach. The examiner has failed to show a motivation, suggestion, or teaching in *Kais* that would lead to the claims of Group I of the applicants' invention. Thus, the examiner has failed to show a *prima facie* case of obviousness.

2. *Kais* Does Not Render Applicants' Invention Obvious Absent Impermissible Arguments.

a. The examiner may not make arguments towards obviousness using impermissible hindsight

The examiner is making impermissible arguments to reach the conclusion that the applicants' invention is obvious in view of *Kais*. First, the examiner must step backward in time into the role of a person of ordinary skill in the art when the invention was unknown and just before it was made. *See* M.P.E.P. § 2142. The Court of Appeals for the Federal Circuit explained:

> A critical step in analyzing the patentability of claims pursuant to section 103(a) is casting the mind back to the time of invention, to consider the thinking of one of ordinary skill in the art, guided only by the prior art references and the then-accepted wisdom in the field. Close adherence to this methodology is especially important in cases where the very ease with which the invention can be understood may prompt one "to fall victim to the insidious effect of a hindsight syndrome wherein that which only the invention taught is used against its teacher."

In re Kotzab, 217 F.3d 1365, 1369; 55 U.S.P.Q.2d (BNA) 1313, 1316 (Fed. Cir. 2000) (citations omitted).

The examiner has argued that the applicants' invention is obvious in view of *Kais*. However, *Kais* does not teach or suggest two coatings that both have the ability of rapid release in the stomach of a patient. It is the examiner's position that *Kais'* disclosure of pH sensitive coatings, and particularly Eudragit E make this aspect of the applicants' invention obvious. But *Kais* gives only very broad categories of acceptable coatings, *i.e.* C_{14-18} fats, C_{16-20} fatty acids, polyol polyesters, C_{14-18} fats and waxes, pH sensitive polymers, food gums, and combinations thereof. This allows a vast number of potential combinations for two coatings. And *Kais* gives no reason to select one coating over another or describes a need to make sure the taste masking coating is

insoluble in neutral to basic pH. The only way *Kais* could arrive at the invention would be through serendipity after undue experimentation or by using the instant application as a roadmap. Nothing in *Kais* teaches a pH sensitive coating on the outer layer, and a pH sensitive coating in the inside layer. Only hindsight would allow one skilled in the art to use *Kais* as an obvious reference to find the applicants' invention.

b. The examiner may not make arguments towards obviousness using an "obvious to try" rationale

The examiner may also not use an "obvious to try" rejection against the applicants' invention as being obvious in view of *Kais*. The Court of Appeals for the Federal Circuit has stated:

> The admonition that "obvious to try" is not the standard under §103 has been directed mainly at two kinds of error. In some cases, what would have been "obvious to try" would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful. In others, what was "obvious to try" was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it.

In re O'Farrell, 853 F.2d 894, 903; 7 U.S.P.Q.2d 1673, 1681 (Fed. Cir. 1988) (citations omitted).

The first type of error is applicable here. In order for one skilled in the art to use *Kais* to get to the applicants' invention, they must vary the coatings with no indication of what parameters are critical, and further still, a direction suggested to use pH sensitive coating that will dissolve in basic environments. Nonetheless, this type of argument is an error and cannot be relied upon by the examiner.

Without using hindsight or trying to vary all the parameters, *Kais* does not obviate the Applicants' invention. *Kais* must stand on its own, with nothing that will make it obvious to have two coatings selected that complement one another in masking the taste and being able to release rapidly in the stomach. The examiner's rejection, with respect to the claims of Group I, is in error.

B. Groups II, III, IV, V and VI

The claimed invention is unobvious for all of the reasons described above in Section VIIIA relating to the claims of Group I. The claims of Groups II, III, IV, V and VI are all dependent upon the independent claims in Group I and therefore, the claims of these groups include all the

limitations of the respective independent claims. Thus, if Group I is unobvious over *Kais*, then Groups II, III, IV, V and VI are also unobvious over *Kais*. However, the claims of these groups are separately patentable, even if the Board adopted the examiner's position as to the claims of Group I.

The claims of Group II include limitations directed to the size of spacing and taste masking layers measured as the increase in the weight of the core. The claims of Group III include limitations as to the thickness of the spacing layer and taste masking layer, for example, between about 5 microns and 30 microns. The claims of Group IV require that the cores of the coated particles be present in a specific percentage based on weight of the finished dosage forms, for example, greater than zero and about 75 percent. The claims of Group V contain requirements that disintegrants and excipients be present in a specific amount based on weight of the finished dosage form, for example, greater than zero and about 75 percent. The claims of Group VI requires that the drug containing cores have a diameter of no larger than a specific size, for example 1200 microns.

The examiner admits that the limitations of Groups II, III, IV, V and VI are not taught by *Kais*. Nevertheless, the examiner rejected the claims of Groups II, III, IV and V stating that the limitations of these claims would be routinely determined by one of ordinary skill in the art, through minimal experimentation, as being suitable, absent the presentation of some unusual and/or unexpected results. The examiner separately rejected the claims of Group VI stating that it is possible that the coated particles of *Kais* are the same as those of the applicants' invention. The examiner further argues that the lack of detail regarding size is an indication that the particle size of *Kais* is a manipulatable limitation determined as part of the process of normal optimization.

The examiner has admitted that the art of record does not disclose the additional limitations of the claims of Groups II, III, IV, V and VI. There is no objective evidence in the record to support the examiner's contentions relating to these limitations. Instead, the examiner has tried to bridge the divide between the applicants' invention and the art of record by making impermissible arguments; namely obvious to try arguments, and arguments of hindsight and inherency, none of which are availing.

The "obvious to try" argument is unavailing (the standards for an obvious to try rejection are discussed above in Section VIII.A.2.b) because for example, for *Kais* to arrive at the limitations of Group II one would have to try varying the size of two separate coatings, and there is no teaching with respect to this limitation in *Kais*. Moreover, *Kais* does not even disclose the

objective or provide an endpoint encompassed within the claimed invention. Thus, even if one would know how coatings thickness can be varied in general, they would have no direction telling them how to achieve the claimed invention. This allows the range of sizes for coatings to be almost infinite. The same is true for the claims of the other groups; one would have to vary a limitation as required in each individual claim with no teaching or suggestion of where to start or end and what would be a successful result. For Group III, one would have to vary the thickness of two separate coatings with no teaching to help suggest where to start or end. Group IV requires the cores to be of a specific weight of the final dosage form. Group V requires that the disintegrant and excipient be present in a specific amount, and Group VI requires that the drug containing core be of a certain size. There is no evidence on the record that supports a rejection of these claims, especially from an obvious to try perspective.

With no evidence in the art of record for the limitations of Groups II, III, IV, V and VI, the examiner implicitly resorted to the applicants' application itself. This is impermissible hindsight, which also does not support obviousness as stated above in Section VIII.A.2.a. An examiner may not use the applicants' own disclosure to piece together a rejection of these claims. The examiner needs to put into the record a basis that can be supported for rejecting the claims, and that has not been done here. Instead, a broad assertion was made to reject a number of claims.

The examiner also argued, particularly for Group VI, that the rejection was based on a normal process of optimization. Optimization is also an unavailing argument because it does not place objective evidence into the record and is based on inherency. The Court of Appeals for the Federal Circuit has stated:

> While the condition described may be an optimal one, it is not "inherent" in Awamoto. Nor are the means to achieve this optimal condition disclosed by Awamoto, explicitly or implicitly. "The mere fact that a certain thing *may* result from a given set of circumstances is not sufficient [to establish inherency.]" "That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown. Such a retrospective view of inherency is not a substitute for some teaching or suggestion supporting an obviousness rejection.

In re Rijckaert, 9 F.3d 1531, 1533-34 (Fed. Cir. 1993) (citations omitted).

There is nothing on the record to direct one to the parameters to be optimized or to suggest where to start. Indeed, *Kais* does not even teach the need for rapid release in the stomach. So how would one of skill ever know what to shoot for when optimizing? Assuredly had the objective been

different, so to would have been the construction of the dosage forms as well as the optimum levels necessary to achieve that alternate objective.

There is nothing implicit or explicit in *Kais* that teaches the limitations of Groups II, III, IV, V and VI. The examiner has admitted that *Kais* does not teach the limitations, and therefore relied on impermissible arguments to reject those claims. Thus, the rejection of these claims based on an obviousness rejection over *Kais* must fail.

IX. CONCLUSION

For the reasons set forth above, this Honorable Board should reverse the rejections of claims 1, 4-18 and 21-25 on appeal.

Dated: October 21, 2003

Respectfully submitted,

By _____

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APPENDIX A

A copy of the claims on appeal is set forth below.

1. A taste masked formulation which rapidly releases in the stomach of a patient comprising:

a drug-containing core;

a taste masking layer composed of a material which is generally insoluble in saliva at a neutral to basic pH and completely soluble in saliva at a pH of less than about 6.5; and

a spacing layer surrounding said core and substantially completely sequestering said core from said taste masking layer and being capable of rapidly exposing said core when exposed in the stomach of a patient; said taste masking layer preventing exposure of said spacing layer in the mouth of a patient for a period of at least about 20 seconds after being placed into the mouth and being capable of rapidly exposing said spacing layer when in the stomach of a patient; wherein the taste-masked formulation disintegrates in the mouth of a patient in less than 90 seconds to form a suspension of particles; wherein the coated drug-containing core generally has a diameter of no larger than 1,500 microns.

4. The formulation of claim 1 wherein said spacing layer is a controlled release material which allows for drug dissolution from the core in a desired release pattern including, but not limited to steady, pulsitile, delayed or targeted.

5. The formulation of claim 1 wherein said drug is a pharmaceutically active material, a vitamin, a mineral, a nutritional supplement and mixtures thereof.

6. The formulation of claim 1 wherein said spacing layer increases the weight of the core by between about 5 and about 100 percent by weight.

7. The formulation of claim 6 wherein said spacing layer increases the weight of the core by between about 20 and about 50 percent by weight.

8. The formulation of claim 1 wherein said spacing layer has a thickness of between about 5 and about 75 microns.

9. The formulation of claim 8 wherein said spacing layer has a thickness of between about 5 and about 30 microns.

10. The formulation of claim 1 wherein said taste masking layer increases the weight of the core by between about 5 and about 100 percent by weight.

11. The formulation of claim 10 wherein said taste masking layer increases the weight of the core by between about 20 and about 70 percent by weight.

12. The formulation of claim 1 wherein said taste masking taste masking layer has a thickness of between about 5 and about 75 microns.

13. The formulation of claim 12 wherein said taste masking layer has a thickness of between about 5 and about 30 microns.

14. A dosage form intended for direct oral administration, comprising:

an effective amount of at least one drug, said drug present in the cores of coated particles, said cores including a taste masking layer composed of a material which is generally insoluble in saliva at a neutral to basic pH and completely soluble in saliva at a pH of less than about 6.5; and

a spacing layer surrounding said core and substantially completely sequestering said core from said taste masking layer and being capable of rapidly exposing said core when exposed in the stomach of a patient; said taste masking layer preventing exposure of said spacing layer in the mouth of a patient for a period of at least about 20 seconds after being placed into the mouth and being capable of rapidly exposing said spacing layer when in the stomach of a patient; and

at least one pharmaceutically acceptable excipient provided in an amount of between greater than zero and less than 100%, based on the weight of the finished dosage form; wherein the taste-masked formulation disintegrates in the mouth of a patient in less than 90 seconds to form a suspension of particles; wherein the coated drug-containing core generally has a diameter of no larger than 1,500 microns.

15. The dosage form of claim 14 wherein said coated particles are present in an amount of between greater than zero and about 95% by weight based on the weight of the finished dosage forms.

16. The dosage form of claim 15 wherein said coated particles are present in an amount of between greater than zero and about 75% by weight based on the weight of the finished dosage forms.

17. The dosage form of claim 14 further comprising a disintegrant wherein the amount of said disintegrant and said excipient are between greater than zero and about 95% by weight based on the weight of the finished dosage forms.

18. The dosage form of claim 17 wherein said disintegrant and said excipient are present in an amount of between greater than zero and about 75% by weight based on the weight of the finished dosage forms.

21. The dosage form of claim 14 wherein said spacing layer is a controlled release material which allows for drug dissolution from the core in a desired release pattern including, but not limited to steady, pulsitile, delayed or targeted.

22. The taste masked formulation of claim 1, wherein the coated drug-containing core has a diameter of no larger than 1200 microns.

23. The taste masked formulation of claim 22, wherein the coated drug-containing core has a diameter of no larger than 850 microns.

24. The dosage form of claim 14, wherein the coated drug-containing core has a diameter of no larger than 1200 microns.

25. The dosage form of claim 24, wherein the coated drug-containing core has a diameter of no larger than 850 microns.

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